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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/087,252	03/01/2002	Peter Leskovar	07038.0003U2	5111
23859	7590	03/16/2005	EXAMINER	
NEEDLE & ROSENBERG, P.C. SUITE 1000 999 PEACHTREE STREET ATLANTA, GA 30309-3915			NICKOL, GARY B	
		ART UNIT	PAPER NUMBER	
		1642		

DATE MAILED: 03/16/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	10/087,252	LESKOVAR, PETER
	Examiner	Art Unit
	Gary B. Nickol Ph.D.	1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

**A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM
 THE MAILING DATE OF THIS COMMUNICATION.**

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 10 January 2005.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-12 is/are pending in the application.
- 4a) Of the above claim(s) 2-6 and 8 is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1,7 and 9-12 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| | 6) <input type="checkbox"/> Other: _____ |

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Re: Leskovar, P.

Date of Priority: 04/15/1988

Response to Amendment

The Amendment filed 01-10-2005 in response to the Office Action of 07-14-2004 is acknowledged and has been entered.

Claims 10-12 were added.

Claims 2-6, and 8 have been withdrawn from further consideration by the examiner under 37 CFR 1.142(b) as being drawn to non-elected inventions.

Claims 1, 7, and 9-12 are currently under consideration.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Claims 1 and 9 remain rejected under 35 U.S.C. 102(b) as being anticipated by Rosenberg *et al.* (Science, Vol. 233, September 1986, pages 1318-1321).

Applicants argue (Response, page 6) that the prior art does not specifically teach eliminating both proliferating and mature suppressor cells (as amended) because it was well known in the art that the cytotoxicity of cyclophosphamide was due to its effect on rapidly proliferating cells. As evidence, applicants point to the teachings of Mastrangelo *et al.* (cited previously) which states that cyclophosphamide “appeared to be working by preventing the

development of mature suppressor cells, possibly by selective toxicity for a ‘presuppressor’ cell (Mastrangelo *et al.*, page 191, col.2, paragraph 1). Applicants further provide an abstract by Adatia, AK which states that “[i]t would seem that of the rapidly proliferating epithelial and mesenchymal odontogenic cells in the basal are of the rat incisor, those in the mesenchyme may be most susceptible to the cytotoxicity of cyclophosphamide.” Applicants interpreted this statement as recognition by Adatia, A.K. that cyclophosphamide was cytotoxic to rapidly proliferating cells, not mature (non-proliferating cells).

These arguments have been carefully considered but are not found persuasive as the provided references are not supportive of applicants assertion that it was well known in the art that cyclophosphamide was selectively cytotoxic to proliferating suppressor cells. First, the extracted passage in Mastrangelo *et al.* does not refer to the addition of cyclophosphamide, but rather the addition of 4-HPCY, (4-Hydroperoxy-cyclophosphamide) a derivative of cyclophosphamide. Thus, applicants are assuming that the addition of a chemically distinct compound like cyclophosphamide to suppressor cells will mimic the effects of 4-HPCY on suppressor cells. This assumption, however, does not extrapolate to a “fact” or otherwise what was well known in the art with regards to cyclophosphamide. Moreover, in the following paragraph, Mastrangelo *et al.* go on to point out that “Although these data are interesting, they must be interpreted with caution, because *in vivo* conditions may be quite different from the *in vitro* environment. In the experiments of Ozer *et al.*, lymphocytes were exposed to a single active metabolite of CY (cyclophosphamide). Yet the plasma of animals and humans who have received a dose of Cy also contains phosphoramide mustard, acrolein, and possibly other as yet unidentified cytotoxic compound.” Thus, it could not be said with absolute certainty, that

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cyclophosphamide is selectively cytotoxic to proliferating suppressor cells based solely on the *in vitro* data generated by Ozer *et al.* Secondly, with regards to the abstract by Adatia, AK, the reference makes no mention of the effects of cyclophosphamide on suppressor cells. Hence, the abstract is not relevant to the claimed method and only suggests (i.e. "it would seem that of the rapidly proliferating cells..") that certain rapidly proliferating cell types of the mesenchyme may be susceptible to the cytotoxicity of cyclophosphamide. Thus, applicant's arguments have not been found persuasive, and the rejection is maintained.

Claims 1, 7, and 9 remain rejected and new claims 10-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rosenberg *et al.* (Science, Vol. 233, September 1986, pages 1318-1321) in combination with the teachings of Berd *et al.* (Cancer Research, Vol. 47, May 15, 1987, pages 2727-2732) for the reasons set forth above and for the reasons of record.

Applicants argue (Response, page 9) that nowhere has it been shown or argued that those of ordinary skill in the art had any general knowledge relevant to eliminating "proliferating and mature (non-proliferating) suppressor cells" in conjunction with adoptive immunotherapy. However, because applicant's arguments are based solely on the amended and new claim terminology, all such arguments are deemed irrelevant and cannot be considered. Thus, applicant's arguments have not been found persuasive, and the rejection is maintained.

No claim is allowed.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary B. Nickol Ph.D. whose telephone number is 571-272-0835. The examiner can normally be reached on M-Th, 8:30-5:30; alternate Fri., 8:30-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gary B. Nickol Ph.D.
Primary Examiner
Art Unit 1642

GBN



GARY NICKOL
PRIMARY EXAMINER